

DNA electronics

DNA and electronics seem to be two different things, but a series of events has highlighted the unusual ability of DNA to form electronic components

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DNA, the blueprint of life, has taken centre stage in biological research during the past few decades. The elucidation of the molecule's structure 50 years ago and the unravelling of the genetic code revolutionized the field of biotechnology. They sparked the creation of whole new industries based on this knowledge and on the various tools and technologies that have subsequently developed. Biologically, the well-known function of DNA is to code for functional proteins that are the expressed form of hereditary, genetic information. But in the past few years, the discovery that DNA can conduct an electrical current has made it an interesting candidate for other roles that nature did not intend for this molecule. In particular, DNA could be useful in nanotechnology for the design of electric circuits, which could help to overcome the limitations that classical silicon-based electronics is facing in the coming years.

In general, DNA electronics does not aim to make something new. Its immediate goal is to improve old concepts in a new manner, although in the process it may create entirely new ideas in nanoelectronics. This field is highly interdisciplinary, merging physics, biology, chemistry, computer science, engineering and so on, to use individual DNA molecules for producing a new range of electronic devices that are much smaller, faster and more energy efficient than the present semiconductor-based electronic devices.

The basic unit of an integrated circuit, such as a computer processor or a memory chip, is the transistor, a simple electronic switch that is etched into various layers of silicon. Alien atoms, added during the production process, allow a transistor to switch between a

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conducting and a non-conducting state, hence the name 'semiconductor'. A modern microprocessor, such as the Pentium IV® chip, has more than 40 million transistors on a silicon chip that is only slightly larger than a thumbnail. The smaller these transistors are, the more can be squeezed onto a chip, thus increasing speed and efficiency. But further miniaturization of transistors is heading towards physical, technical and economic limits, and these limits will be reached within a few years (Peercy, 2000). Beyond a certain limit, the number of silicon atoms in the insulating layers of a transistor is no longer sufficient to prevent the leakage of electrons that causes the circuit to shorten (Kington *et al.*, 2000). In addition, the cost of production increases drastically with any reduction in size. To overcome these limitations, researchers in the computer industry have been looking into materials other than silicon that would allow them to pack even more transistors into a given space. Rapid advances that explore such alternative technologies have taken place during the past years, including polyphenylene-based diode switches and carbon nanotube field-effect transistors (Bachtold *et al.*, 2001). But these approaches still face many technical challenges. Nanotubes, for instance, have to be grown to a high specification as each tube has different electrical properties depending on its diameter and helicity.

The techniques available yield only tubes of variable proportions. So the need to develop even smaller electronic devices may eventually lead us into the domain of DNA electronics. In fact, DNA offers a solution to many of the hurdles that need to be overcome. It is the best nanowire in existence, and it self-assembles, self-replicates and can adopt various states and conformations. Of these, the most important property of DNA for a biomolecular engineer is its ability to self-assemble, which makes it possible to produce nanostructures with a precision that is not achievable with classical silicon-based technologies (Winfrey *et al.*, 1998). And it is cheap, as the cost of individual bases is just a few US cents.

The beauty of DNA electronics lies in the fact that it uses the techniques of genetic engineering that nature has perfected under harsh conditions over billions of years. The idea of using organic molecules for building electronic components dates back to 1974 (Aviram & Ratner, 1974), but the study of the electrical properties of DNA goes back even further. The structure of DNA was discovered by Watson and Crick, who received a Nobel Prize for their work in 1962. The question of whether the molecule could be used as an electrical conductor or insulator was ripe even at that time, but the technology was not. Measuring the electrical current through DNA is not as easy as connecting two wires to make a light bulb glow, and it requires sophisticated instrumentation, such as atomic force microscopy and optical tweezers to align a single DNA molecule on a micro- or nanoelectrode. Above all, these

experiments need a highly sensitive system for measuring current voltage and capacitance voltage, which are important parameters that describe the performance of an electronic device, to measure current in the femto (10^{-15}) ampere range.

To bind a single DNA molecule to an electrode is a tough job, and difficulties also arise in validating whether the two are actually connected (Fig. 1). But the effort pays off, because DNA has been shown to act as an insulator, a semiconductor, a conductor or a proximity-induced superconductor depending on its sequence, length and orientation. However, these experiments were carried out by different research groups, and it is difficult to draw firm conclusions about the transport of electrical charge through DNA due to the variety of surrounding conditions used (Hippis, 2001).

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Fink & Schonenberger (1999) were the first to measure current flow through DNA using a modified low-energy electron point-source microscope. Their technique used a gold-coated carbon grid as the sample holder, consisting of an array of 2- μm holes and 600-nm-long λ -DNA to span these holes. A tungsten manipulation tip was used to contact the sample and to allow electric current to flow. The authors measured linear current voltage (I/V) curves in the range of -20 to $+20$ mV, and a resistance of $2.5 \text{ M}\Omega$ per DNA molecule at room temperature. Various other studies have confirmed that DNA can act as a molecular wire, with the phosphate bonds in the DNA backbone acting as tunnel junctions for electrons to move along.

More recently, a Dutch team has shown that a 10.4-nm-long (30-base-pair) poly(G)-poly(C) sequence has electrical characteristics similar to that of a semi-conducting diode that allows current to flow in one direction only (Porath *et al.*, 2000). The authors measured I/V curves in the range of -4 to $+4$ V and found that the measured current flow did not fall more

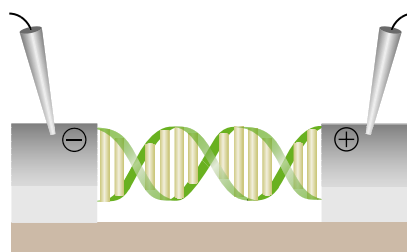


Fig. 1 | Experimental design for making electrical measurements with DNA. A DNA strand spans two metallic electrodes on a non-conducting surface. By using manipulation tips on those electrodes, investigators can measure current flow through the DNA molecule.

than 1 pA below a certain threshold value. In this voltage range, DNA behaved as an insulator. Beyond the threshold voltage, the current increased sharply, indicating that DNA conducts charge and thus behaves in the same way as the silicon-based semiconductors used in the electronics industry. However, the experiment is prone to criticism as the researchers used electrostatic trapping techniques (Bezryadin *et al.*, 1997) and did not create chemical bonds between the DNA and the electrodes. Other researchers reported that DNA also behaves like a proximity-induced superconductor (Kasumov *et al.*, 2001), using 16 μm of λ -DNA to connect two rhenium carbon electrodes on a mica substrate.

The conductivity of DNA can be increased by coating it with metals in various ways. Braun and colleagues (1998) used the self-assembly property of DNA to synthesize a molecule between two electrodes that were 12 μm apart; the DNA molecule was then used as a template for the deposition of silver to create a 100-nm-wide conductive wire. The contact between the DNA and the gold electrodes was thiol-mediated, as gold has a natural affinity for sulphur and 3'-thiolated DNA primers can be routinely created. Nowadays, the preferred technique for such an approach is to, first, bind short primer sequences to gold electrodes, and then to use restriction sites in the primers to complete the circuit with an interspersing DNA molecule. Aich and co-workers (1999) went one step further and showed that DNA with zinc atoms incorporated between its bases also acts as a conductor. Other metals, such as nickel and cobalt,

can similarly be used. On the basis of these results, DNA has the potential to self-assemble to form any circuit and to function as a template for the deposition of metal atoms. It also allows certain sites to be protected from metal deposition by masking them with sequence-specific DNA-binding proteins. Such molecular lithography has already been carried out using the RecA protein, which further increases the potential of using DNA for the chemical 'growth' of electronic parts (Keren *et al.*, 2002).

The unique structure of DNA also allows various alterations to its material properties, such as its sequence, diameter and stiffness, which could all modify its electrical properties. While exploring the potential of DNA as an electric wire, we found that guanine is the base with the lowest oxidation potential (Bharadwaj *et al.*, 2002a). It loses an electron during oxidative stress and becomes positively charged. This positive charge does not stay at the base where it was formed, but keeps moving along G-rich sequences. Indeed, G-rich sequences lower the molecule's oxidative potential, so a positive charge can move from a single guanine towards a multiple guanine sequence that attracts such electron holes (Saito *et al.*, 1998).

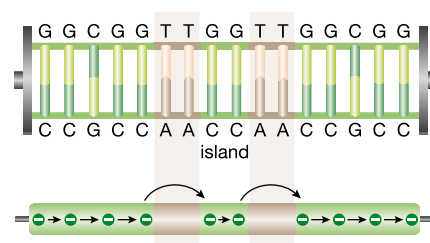
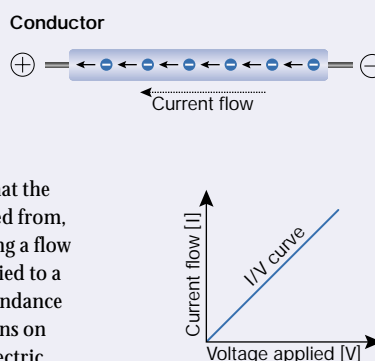


Fig. 2 | A hypothetical resonant tunneling diode based on DNA. It consists of guanine/cytosine-rich donor and acceptor sequences at the poles, which are interrupted by two adenine/thymine-rich sequences and a short island of guanine and cytosine. In a silicon-based resonant tunneling diode the barriers between the conducting parts stop current from flowing. Above a certain voltage, electrons can jump over the barriers through the small island and current begins to flow. In a DNA-based resonant tunneling diode, the guanine/cytosine sequences would accept electrons from the negative pole that could, beyond a certain breakthrough voltage, jump through the island over the adenine/thymine barriers to allow electrons flow to the positive pole.

PRINCIPLES OF ELECTRONIC DEVICES

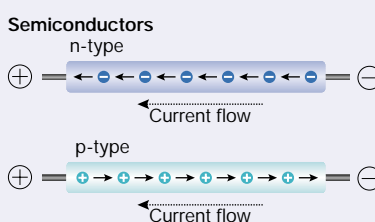
An electrical conductor, such as a metal or a carbon wire, has the ability to transfer electrons from a source with a high abundance of free electrons to an electron 'hole', which accepts free electrons, such as happens at the negative and the positive poles of a car battery.

The ability to transfer free electrons is due to the fact that the outer electrons of atoms in a metal can be easily stripped from, and wander between, neighbouring atoms, thus allowing a flow of electrons along the wire. The higher the voltage applied to a wire—that is, the greater the potential between the abundance of electrons on the negative pole and the lack of electrons on the positive pole—the more electrons, and therefore electric current, flow through the wire, thus creating the characteristic linear I/V curves.

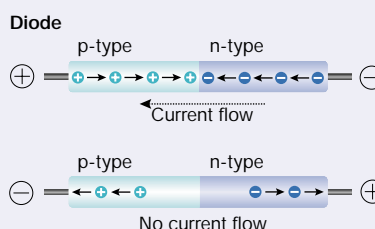


In a semiconducting material, such as silicon, the outer electrons of the atoms can be replaced, albeit not as easily as in a metal. But doping silicon—carefully impurifying it with alien atoms during the production process—creates additional free electrons that can be displaced to neighbouring atoms and thus transfer charge.

A semiconducting material with excess electrons is named an n-type semiconductor. Similarly, a p-type semiconductor is doped with atoms that lack electrons, and which therefore create electron holes in the material. On applying voltage to a p-type semiconductor, these electron holes move from the positive pole to the negative, and a net current flows in the opposite direction.



The combination of n- and p-type material is the basis for creating the diodes and transistors that are the elements of an electronic circuit. For instance, a diode consists of a combination of n-type and p-type materials that touch at some point. By applying voltage in the right direction, electrons move from the negative pole to the contact site, where they merge with electron holes coming from the positive pole and allow current to flow. By reversing the applied voltage, the electrons in the n-type material and the electron holes in the p-type material move away from the merging point towards their respective poles and no net current flows. Diodes thus act as electronic valves that allow current to flow in one direction only.



A transistor is a more complex version of a diode that allows current to flow in a defined direction but that also acts as an electronic on-off switch. It is switched on by current flow from a third pole, which switches it off again if the current flow from this pole ceases.

In general, n-type material uses negatively charged electrons to carry current, whereas positive p-type material uses electron holes to do so. Joining the two types allows the current to flow in a specified direction, which is the basis for all semiconductors, such as diodes, triodes and transistors (Fig. 2). (G+C)-rich DNA shows p-type properties and (A+T) sequences show n-type ones (Lee *et al.*, 2002). Combining such DNA molecules

could create logic elements that would be more powerful than any silicon-based device because, in theory, just a short sequence of DNA base pairs may be enough to create all the combined n- and p-type properties. Indeed, DNA-based single-electron transistors and quantum-bit elements have already been proposed (Ben-Jacob *et al.*, 1999). For more information, see the sidebar.

Gordon Moore, from the Intel Corporation, formulated a law in 1965, now known as Moore's Law, stating that the number of transistors on a chip would double every 18 months, but that this trend would drastically change between 2010 and 2020 when the doubling rate would drop to every 4–5 years. DNA-based electronics has the potential to extend beyond Moore's Law, proclaiming the end of conventional microelectronics. But a computer that is based on DNA molecules—it could be labelled 'Genes Inside'—is still a long way off. To design electronic components that consist of DNA molecules, we first need more detailed knowledge of the mechanism of charge transfer through DNA and its exact electrical characteristics. Indeed, the mechanism by which DNA transports a current is still unknown, although we already know that pi electrons in the chemical bonds are important. Furthermore, a DNA-based computer chip, even if it becomes reality, may not be totally based on DNA. We are actually heading towards a hybrid technology, in which the transistor could be made out of DNA molecules that are connected by carbon nanotubes, and other parts would be made out of silicon.

Even though the use of DNA for electronics seems to be a distant goal, the first biological research applications using the electrical properties of DNA could appear in the next few years. For instance, we could detect mismatches in double-stranded DNA because such a mismatch would hamper conductivity, which is sensitive at the level of single bases. Similarly, it could be used for routine single-nucleotide polymorphism detection and mutation analysis (Park *et al.*, 2002) and, with further advances in this field, it could allow the use of DNA-based electronic sensors and, thus, DNA-based diagnostics. The study of the electrical properties of DNA also promises further advances in understanding DNA-repair processes and DNA-damage chemistry, and their correlation with disease and the process of ageing. DNA damage is induced by ultraviolet radiation or oxidative stress, causing oxidation of guanine, and electron holes then migrate along the DNA molecule. Similarly, DNA repair takes place by electron transfer from the enzyme photolyase to thymine dimers to initiate the photorepair process.

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But, first, we have to overcome the current limitations. Much of the work on charge transfer in DNA and the study of its electrical characteristics has been inconclusive because we lack suitable techniques and instrumentation. To make authentic electrical measurements on DNA, it is imperative that we have control over its orientation, bending, length and sequence, and over the contamination between electrodes. The sequence and length of DNA can be accurately controlled during its synthesis. The challenge now is to control bending, orientation and contamination at the molecular level, and that is where we face limitations of technology and knowledge. These are important factors as the flow of current through DNA can change considerably due to slight changes in the relative positions of pi orbitals by bending, orientation and overlapping. Control over all these parameters using a single technique is not feasible during electrical measurements; instead, a multi-technique approach is required to achieve reasonable reproducibility. For instance, our group is developing an integrated approach based on scanning probe microscopy, scanning electron microscopy, optical tweezers, current-voltage and capacitance-voltage measurement in the femto range, and fluorescence microscopy. The biggest challenge will be to control contamination at the molecular level while integrating DNA fragments into electronic devices.

If we compare the exponential growth in computing power to the development of the human brain during evolution, today's computers have a similar complexity to that of a tiny insect. So, will it really be possible to match the computing power of the human brain one day? If that is to happen, it could only be by means of adopting the structures developed in nature. DNA electronics, which takes inspiration from

nature and genetic engineering, will probably enable more powerful and environmentally friendly technologies. DNA could be used to replace not only conventional transistors, but also memory devices (Bharadwaj *et al.*, 2002b), as one cubic centimetre of DNA can store more information than trillions of compact discs. Clearly, the days when DNA was the domain of the biologist are over.

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